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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/017,216	10/23/2001	Rosana Kapeller-Libermann	10147-57U1 (MPI2000-513P1)	1141

7590 09/02/2004

Intellectual Property Group
Millennium Pharmaceuticals, INC.
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EXAMINER

MONSHIPOURI, MARYAM

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 09/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/017,216	KAPELLER-LIBERMANN, ROSAN	
	Examiner	Art Unit	
	Maryam Monshipouri	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8,12,13,16-18,23,39,45 and 48 is/are pending in the application.
- 4a) Of the above claim(s) 8,13,16,17,23,39,45 and 48 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 2 is/are allowed.
- 6) ☒ Claim(s) 1,3-7,12 and 18 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. ____. |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>2/12/02&9/3/02</u> . | 6) <input type="checkbox"/> Other: ____. |

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Applicant's response to restriction requirement filed 6/14/2004 is acknowledged.

Applicant elected Group I invention (directed to claims 1-7, 12 and 18) without traverse.

Claims 8, 13, 16-17, 23, 39, 45, 48 are withdrawn as drawn to non-elected invention.

Claims 9-1, 14-15, 19-22, 24-38, 40-44, 46-47, 49 are canceled.

DETAILED ACTION

Claims 1-7, 12 and 18 are under examination on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3-7, 12 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "stringent conditions" in claim 1 (and its dependent claims 3-7, and 18) as well as claim 12 is unclear. Applicant has not specifically defined this term in the specification but merely provided some preferred salt and temperature conditions which may be used for stringent hybridization conditions. In the absence of a clear recitation of exact salt and temperature conditions used for stringent hybridization in claims 1 and 12 the skilled artisan does not know how to prepare the claimed nucleic acid molecules.

Claims 1, 3-7, 12 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "naturally occurring allelic variant" is unclear. In page 15, applicant defined the term "naturally occurring nucleic

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acid' as referring to an RNA or DNA molecule that occurs in nature; and in page 24 he/she defines the term "allelic variants" to include both functional and non-functional proteins. He/she further defined functional allelic variants as those that contain only conservative substitutions of one or more amino acids of SEQ ID NO:2, or contain mutation of non-critical residues in non-critical regions of the protein wherein said variants maintain the biological activities described in the specification. According to applicant, non-functional allelic variants will typically contain non-conservative substitutions, deletions, insertions or premature truncations of SEQ ID NO:2, or those that contain mutations in critical residues or critical regions of the protein and do not have the ability to mediate biological activities of SEQ ID NO:2. Based on said definitions the following questions remain unanswered: **(1)** How many amino acids constitute the word "more" in definitions provided for functional and non-functional variants. For example, up to how many amino acids in 2053 amino acids of SEQ ID NO:2 may be substituted before said variant turns structurally from functional into non-functional variant. **(2)** what are the critical and non-critical regions of SEQ ID NO:2; **(3)** what biological activities beyond kinase activity is applicant referring to for variants; **(4)** up to how many conservative/non-conservative amino acid mutations in a variant will still allow categorizing said variant as "naturally occurring". After all, applicant has not disclosed all possible structures of SEQ ID NO:2 "naturally occurring allelic variants" so that they could be used as a reference for characterizing all claimed variants etc. In the absence of a clear answer to said questions the metes and bounds of said phrase is unclear.

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The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1,3-7, 12, 18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for isolated nucleic acid molecules encoding ATM related kinases of SEQ ID NO:2, does not reasonably provide enablement for any of the following:

(a) isolated nucleic acid molecules comprising a DNA sequence which is at least 60% identical to SEQ ID NO:1 and 3, with no function.

(b) isolated nucleic acid molecules which comprise at least 300 nucleotides of SEQ ID NO:1 and 3 and isolated nucleic acid molecules encoding a fragment of SEQ ID NO:2, wherein said fragment comprises at least 15 contiguous amino acids of SEQ ID NO:2 (wherein said DNA fragment must inherently comprise (15X3) 45 bases of said DNA sequences) with no function.

(c) isolated nucleic acid molecules encoding a "naturally occurring allelic variants" of SEQ ID NO:2, wherein the molecule hybridizes with a DNA molecule comprising SEQ ID NO:1, 3 or complement thereof, under stringent conditions, with no function.

The criteria for undue experimentation, summarized in *re Wands*, 8, USPQ2n 1400 (Fed. Cir. 1988) are: 1) the quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence and absence of working examples,

4) the nature of the invention, 5) the state of prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breadth of the claims.

The specification fails to teach any of the following: which critical residues in isolated nucleic acid molecules of **(a)**, **above** must be preserved such that after mutating up to 40% of bases of SEQ ID NO:1 or 3 said sequences are still encoding products that are within the scope of this invention (i.e. retain kinase activity). What other bases beyond 45-300 bases of SEQ ID NO:1 or 3 should be present such that isolated nucleic acid molecules of parts **(b)** still encode products that are supported by the specification (i.e. have kinase activity). After all for any DNA fragment to encode kinase activity it must comprise at least a region of 750 bases to be able to encode the 250 amino acids corresponding to catalytic regions of most kinases. What homologs of SEQ ID NO:1 or 3 (see part (c)) are capable of encoding SEQ ID NO:2 variants that are supported by the specification (see the rejection given for indefiniteness of the phrase "naturally occurring allelic variants", given above. No examples of such nucleic acid molecules are provided either. Current state of the art indicates that once more than 10 bases of a DNA sequence is mutated (see part (a)), many of its residues are missing or are replaced randomly (see part (b)), or lacks sufficient essential structural constituents because the conditions under which they are prepared are unclear (see part (c)), it is almost impossible to predict the function of its expression products.

Therefore due to lack of sufficient guidance and examples provided in the specification and due to unpredictability of prior art one of skill in the art has to go through the burden of undue experimentation in order to screen for DNA sequences that

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have support in the specification and as such the claims go beyond the scope of the disclosure.

Since claim 1 is not enabled, its dependent claims 3-7 and 18 are not enabled either.

Claims 1, 3-7, 12 and 18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 1 (and its dependent claims 3-7, and 18) as well as claim 12 are directed to the following **genera** of DNA sequences that have been inadequately described in the specification.

(a) a genus of isolated nucleic acid molecules comprising a DNA sequence which is at least 60% identical to SEQ ID NO:1 and 3, with no function.

(b) a genus of isolated nucleic acid molecules which comprise at least 300 nucleotides of SEQ ID NO:1 and 3 and a genus of isolated nucleic acid molecules encoding a fragment of SEQ ID NO:2, wherein said fragment comprises at least 15 contiguous amino acids of SEQ ID NO:2 (wherein said DNA fragment must inherently comprise (15X3) 45 bases of said DNA sequences) with no function.

(c) a genus of isolated nucleic acid molecules encoding a fragment of SEQ ID NO:2, wherein said fragment comprises at least 15 contiguous amino acids of SEQ ID NO:2, with no function.

(d) a genus of isolated nucleic acid molecules encoding a naturally occurring allelic variants of SEQ ID NO:1 or 3, that hybridize to SEQ ID NO:1 or 3 under stringent conditions (see the 112 second rejection drafted above), comprising numerous embodiments with no function.

The genera of cDNAs that comprise these above cDNA molecules is a large variable genera with the potentiality of encoding many different proteins. Therefore, many functionally unrelated DNAs are encompassed within the scope of these claims, including partial DNA sequences. The specification discloses only two **species** (namely SEQ ID NO:1 or 3) of each claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

Since DNA sequences of claim 1 are inadequately described, vectors, kits and host cells comprising said sequences are also inadequately described.

Applicant is referred to the revised interim guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3-7, 12 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Di Cunto et al. (J.B.C., 273(45), 29706-29711, 1998, cited in the IDS). Di Cunto teaches a DNA sequence that can hybridize to SEQ ID NO:1 or 3 of this invention under stringent hybridization conditions (see the attached DNA sequence alignment). Di Cunto (see Materials and Methods section) teaches about recombinant plasmids and both COS cells and mouse keratinocytes comprising its DNA sequence, anticipating claims 3-7 as well as methods of expressing said DNA sequence (see page 297097, column 1, protein analysis section). In page 20706, Di Cunto teaches about a CLONETECH kit that comprises a cDNA that can hybridize to a fragment of SEQ ID NO:1 or 3 capable of encoding 15 contiguous amino acids of SEQ ID NO:2 or a fragment of SEQ ID NO:1 or 3, of 300 bases in length, under "stringent hybridization conditions" (see the 112 second paragraph rejection drafted above), anticipating claim 18.

Allowable Subject Matter

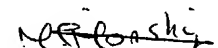
Claim 2 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. This is because DNA molecules comprising sequences encoding full-length SEQ ID NO:2, including SEQ ID NO:1 and 3 are free of prior art. Further, the prior art does not teach or suggest preparing such specifically claimed DNA molecules. Hence, said molecules are also non-obvious.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maryam Monshipouri whose telephone number is (571) 272-0932. The examiner can normally be reached on 7:00 a.m to 4:30 p.m. except for alternate Mondays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnanthapu Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Maryam Monshipouri Ph.D.

Primary Examiner
